

DI -- The quality of dissolution, i.e. the effective dispersion at the molecular level of each lipopeptide before the preparation of the mixture, is confirmed by the two-dimensional nuclear magnetic resonance method (2DNMR). The resolution of the signal obtained during homonuclear experiments in two dimensions in a 600 MHz field confirms the complete dispersion, at the molecular level, of the lipopeptides in solution. The clarity of the mixture is not a sufficient criterion: in particular, the taking up of the lipopeptides by DMSO or a DMSO/water mixture does not lead, in most cases, to a sufficient dispersion state, which explains the ineffectiveness of the mixture studied by VITIELLO et al. (1995, cited above). Dissolution by acetic acid/water mixtures which are more dilute in acetic acid also does not lead in all cases to the preparation of a mixture of mixed micro-aggregates or micelles containing a statistical proportion of each constituent of the mixture at the microvolume level. In these two cases, even in the presence of an apparently clear mixture, the sterilizing filtration over a 0.22 μm membrane is either impossible, or irregular, with filtration yields which differ according to the constituents, which indicates that at the scale of a particle of this size, the representation of each constituent of the mixture has not been achieved. This micro-heterogeneity compromises the immunogenicity of the mixture, since it comprises the simultaneous capture and presentation of all constituents by a single antigen-presenting cell (APC), in the case of CTL and HTL antigenic determinants present on separate lipopeptides.
